1: Hum Immunol 1999 Jul;60(7):583-90 Related Articles, Links



# NOD background genes influence T cell responses to GAD 65 in HLA-DQ8 transgenic mice.

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The major histocompatibility complex (MHC) genes play a significant role in the predisposition to insulin-dependent diabetes mellitus or type 1 diabetes. HLA-DQ8 (DQB1*0302, DQA 1*0301) genes have been shown to have the highest relative risk for human type 1 diabetes. To develop a "humanized" mouse model of diabetes, HLA-DQ8 was transgenically expressed in mice lacking endogenous class II genes. Since non-MHC background genes of the NOD influence the disease process, AP"/DQ8 mice were mated with the NOD strain and backcrossed to generate Abeta degree/DQ8/NOD mice. These mice have DQ8 as the sole MHC class II restriction element with NOD background genes at the N 2 generation. The DQ8 transgenic mice were used to identify T cell epitopes on glutamic acid decarboxylase (GAD 65), an important putative autoantigen in type 1 diabetes. The NOD background genes strongly influenced antigen processing, that is, different T cell epitopes were generated from the processing of GAD 65 in vivo in the Abeta degree/DQ8 and in the Abeta degree/DQ8/NOD mice.

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END OF SEARCH HISTORY

1: Hum Immunol 2002 Nov;63(11):987-99

Related Articles, Links



# Modulation of insulitis and type 1 diabetes by transgenic HLA-DR3 and DQ8 in NOD mice lacking endogenous MHC class II.

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To evaluate the contributions of DR3 and DQ8 to the etiopathogenesis of type 1 diabetes in a diabetes-predisposing milieu, we developed human leukocyte antigen (HLA) transgenic mice on the nonobese diabetic (NOD) background in the absence of the endogenous class II molecule, I-A(g7) and studied the incidence of both spontaneous and experimental (induced) autoimmune diabetes. Transgenic expression of HLA-DR3 and -DQ8 (either alone or in combination) did not confer susceptibility to spontaneous or cyclophosphamide-induced type 1 diabetes. Expression of I-A(g7) was mandatory for development of spontaneous or cyclophosphamide-induced diabetes. However, multiple low doses of streptozotocin could induce diabetes in all groups of mice independent of the class II molecules expressed. In unmanipulated mice, only islets from I-A(g7+/+) mice revealed significant intra-islet infiltration. Although a characteristic peri-insulitis/peri-ductulitis was present in Abeta(0)/NOD mice, islets from DR3, DQ8 and DR3 x DQ8 double transgenic mice demonstrated significantly less infiltration. In conclusion, transgenic expression of HLA-DR3 and -DQ8 associated with predisposition to type 1 diabetes alone is not sufficient to induce spontaneous diabetes in NOD mice lacking endogenous class II molecules.

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